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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,059	12/14/2005	William Marshall Stark	056646-5024	2559
9629 7590 05/27/2010 MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004				
EXAMINER				
CHOWDHURY, IQBAL HOSSAIN				
ART UNIT		PAPER NUMBER		
1652				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/529,059

**Applicant(s)**

STARK ET AL.

**Examiner**

IQBAL H. CHOWDHURY

**Art Unit**

1652

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 4.47.52.54.57-59.67 and 70 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4.47.52.54.57-59.67 and 70 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ ~~Notice of Informal Patent Application~~
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Application Status***

Claims 4, 47, 52, 54, 57-59, 67 and 70 are currently pending in this application.

In response to a previous Office action, a non-final action (mailed on 8/11/2009), Applicants filed an amendment on 2/11/2010, amending claims 47, 52, 54, 57, 58, 59 and 67, canceling claim 46, and adding new claim 70 is acknowledged.

Applicants' arguments filed on 2/11/2010, have been fully considered and are deemed persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 4, 47, 52, 54, 57-59, 67 and 70 are under consideration.

***New-Claim objection***

Claim 57 is objected to in the recitation "M1031", which should be "M103I".  
Appropriate correction is required.

Claim 70 is objected to in the recitation "E124, E124", which should be "E124".  
Appropriate correction is required.

Claim 52 is objected to in the recitation "in Tn3 resolvase (SEQ ID NO: 2)", which should be "in Tn3 resolvase of SEQ ID NO: 2".

Claim 70 is objected to in the recitation "of Tn3 resolvase (SEQ ID NO: 2)", which should be "of Tn3 resolvase of SEQ ID NO: 2".

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 4, 47, 52, 54, 57-59 and 70 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 4 and 70 recite "A serine recombinase" or "A catalytic domain of a serine recombinase" in the context of mutation in said protein or domain, which reads on a naturally occurring polypeptide having natural mutation. Naturally occurring polypeptide is not patentable.

In the absence of the hand of man, naturally occurring nucleic acids and /or proteins are considered non-statutory subject matter. *Diamond and Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated serine recombinase" or "An isolated catalytic domain. For examination purpose the claim is read as such.

***Withdrawn-Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of Claims 46-47, 52, 54, 57-59 and 67 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement and scope of enablement is withdrawn in view of cancellation of claim 46 and adding new claim 70 upon which claims 47, 52, 54, 57-59 and 67 are depend, wherein claim 70 now recites "wherein said catalytic domain consists of at least one additional mutation

selected from the group consisting of V107 --- Tn3 resolvase (SEQ ID NO: 2) in view of closed transition phrase "consists of".

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 47, 52, 59, 67 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Sarkis et al. (A model for the gamma delta resolvase synaptic complex, Mol Cell. 2001 Sep;8(3): 623-31, see IDS).

Sarkis et al. teach a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S, and further comprising mutations E102Y, M103I, E124Q and Q105L having greater recombinase efficiency. Sarkis et al. also teach mutations at 2,3-interface in the catalytic domain, i.e. R2 and E56, wherein E56 mutation is E56K. A kit comprising catalytic domain of claim 70 is nothing but the mutant serine recombinase of Sarkis et al.

Therefore, Sarkis et al. anticipate Claims 47, 52, 59, 67 and 70 of the instant application.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1652

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sarkis et al. (A model for the gamma delta resolvase synaptic complex, Mol Cell. 2001 Sep;8(3): 623-31, see IDS) as applied to claims 47, 52, 59, 67 and 70 above and further in view of Hughes et al. (Protein-protein interactions directing resolvase site-specific recombination: a structure-function analysis, EMBO J. 1993 Apr;12(4):1447-58).

Sarkis et al. teach a mutant serine recombinase Tn3 resolvase comprising a mutation at position G101, wherein the mutation is G101S, and further comprising mutations E102Y, M103I, E124Q and Q105L having greater recombinase efficiency. Sarkis et al. also teach mutations at 2,3-interface in the catalytic domain, i.e. R2 and E56, wherein E56 mutation is E56K. Sarkis et al. do not teach a catalytic domain of

serine recombinase comprising mutation at R2A and E56K in addition to mutation at G101 (p628, left column, paragraph 4-5, Fig. 6 and right column, paragraph 1) .

Hughes et al. teach mutant of  $\gamma\delta$  resolvase having a mutation R2A, which is at the 2,3-interface (p1451, left column paragraph 2 and Fig 8).

Sarkis et al. clearly teach that 2,3-interface of catalytic domain of serine recombinase comprises R2 and E56 (p624, right column, paragraph 1 and Fig. 2, p628 left column, paragraph 5). Hughes et al. teach a specific mutation R2A at the 2,3-interface.

By combining the teachings of Sarkis et al. and Hughes et al. it would have been obvious to one of ordinary skill in the art at the time of the invention was made to make additional mutation at position R2 of recombinase in the modified recombinase of Sarkis et al. which comprises G101S, as Sarkis et al. suggested mutation at 2,3-interface such as R2 and E56K and modify R2 as R2A as taught by Hughes et al. to make a serine recombinase, which might have additive effect on the recombinase activity to arrive the claimed invention.

One of ordinary skill in the art would have been motivated to make a mutation at the 2,3-interface such as R2A and E56K in addition to G101S because 2,3-interface is important to binding to the DNA.

One of ordinary skill in the art would have a reasonable expectation of success because Hughes et al. could successfully made R2A mutation of  $\gamma\delta$  resolvase.

Therefore, claims 54 would have been *prima facie* obvious to use one of ordinary skill in the art.

### ***Conclusion***

#### **Status of the claims:**

Claims 4, 47, 52, 54, 57-59, 67 and 70 are pending.

Claims 4, 47, 52, 54, 57-59, 67 and 70 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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